Three year experiment using polidocanol foam in the treatment of reticular varices and varicose veins

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SUMMARY

[see original]

INTRODUCTION

At the meeting on 14 December 1996, arranged in Paris by the French Phlebology Society, we reported the feasibility, results and complications after a year's daily practice of sclerotherapy on reticular varices and telangiectases using polidocanol foam [1].

This fascinating technique entails creating an air/ sclerosant mix extemporaneously, using the air as a "dilutant" and product "vector". At that time we were among the very few angiologists using this ancient procedure, now updated and enhanced by A. Monfreux, a procedure which was reminiscent to us of the use of sodium tetradecyl sulphate foam which we used in sclerosis of the saphenous arches and trunks in the 1980s.

Since this report in December 1996, using foam has fascinated numerous colleagues which is not surprising as it represents a major advance in the practice of sclerotherapy.

We are now presenting more detailed results of our personal experiment spread over almost three years (early November 1995/end of September 1998), applied to more than 10,000 patients.

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BACKGROUND

This technique is the direct result of work by E.J.Orbach [2] who, as early as 1944, suggested "introducing air prior to injecting the sclerosant, thereby emptying the vessel of its blood content" (a technique known as "air-block") and allowing the sclerosant to remain in contact with the endothelium of the vein for longer without any direct dilution by the blood. He used this method in sclerosis of major varices and saphenous trunks.

He recommended not exceeding the dose of 3 cc of air, referring to the study by H.F.Richardson. The latter had researched (in experiments which it would be very difficult to carry out nowadays!) lethal quantities of intravenously injected air in anaesthetised and non-anaesthetised dogs. His conclusions, published in 1937 [3], state that:

- This lethal volume of air is inversely proportional to the rate of injection and substantial volumes of air remain compatible with life if the rate of delivery of the injection is slow. Thus, a dog weighing 23.5 kg tolerates a rate of delivery of air of 0.033 cc/kg/min for 86 hours (i.e. a total injected volume of 3910 cc) before dying whereas a dog weighing 10 kg with a rate of delivery of 2.14 cc/kg/min died within 7 minutes (total injected volume: just 150 cc);
- Anaesthesia and hypertension increase tolerance to the injection of air;

- The pulmonary capillary bed forms an obstacle to the passage of air. During post mortems on the dogs, the air was found in the lower and upper venae cavae, the right auricle and ventricle and in the pulmonary arteries. It was never found in the left chambers of the heart or in the systemic arteries.
- Air obstruction of the pulmonary circulation was the cause of death from cardiac failure in the animals.

A few years before, in 1934, H.N.Harkins and P.H.Harmon (4) had already evaluated the minimum lethal dose of air introduced into a vein among anaesthetised dogs: 8 cc per kilo of body weight when the total volume is injected within 20-30 seconds. They stated that:

- if the quantity of air remains moderate, the animal usually does not display any sign of pulmonary or cardiac failure;
- if the volume is larger, respiratory distress, cardiac insufficiency and then death occurs sooner or later;
- when the injection is administered very quickly, respiratory distress and death occur almost immediately.

Systemic pressure also appeared to play a part. An animal with low blood pressure tolerated injection of air less well.

A projection for humans based on the results from H.N.Harkins and P.H.Harmon therefore indicates that a volume of 480 cc of air entering into the veins within 20-30 seconds would cause death in a subject weighing 60 kilos.

In 1950, E.J. Orbach (5) recalled his air-block technique, which allowed him to "achieve a 10% improvement in the success rate of sclerotherapy," and states that following various experiments conducted using "soapy" agents, he successfully used 3% sodium tetradecyl sulphate foam obtained by energetically shaking the bottle. However, this only converts 20% of the sclerosant into foam with bubbles of a relatively large (3-7 mm) and irregular calibre. He also described a variant involving injection, after the foam, of a small quantity of undiluted sclerosant (around 0.1-0.4 cc).

In 1995, A. Monfreux reported, in the form of a video cassette, the results of his experiment with polidocanol foam in sclerosis of varices, obtained in a very straightforward way: all the sclerosant (pure or undiluted) is converted into small calibre micro-bubbles.

Attracted by the ingenious, innovative nature of this technique, we immediately applied it (early November 1995), first to sclerosis of reticular varices and varicose veins and then very soon, owing to the excellent results achieved, to our sclerotherapy work (arches, trunks, deformities, etc). In fact, the foam produces a sclerosis that is in every respect comparable to that achieved using the solution but requires far less sclerosant, thereby causing less frequent and less intense adverse effects (inflammatory reactions, thromboses, local pigmentation, etc).

TECHNIQUE

Currently the foam can only be produced using glass syringes. We prefer 3 cc syringes with an eccentric tip. Following the procedure outlined by A. Monfreux for reticular varices and varicose veins, we draw up into the syringe between 0.3-0.4 cc of 0.5% polidocanol solution to which we add 0.1-0.2 cc of physiological serum, depending on the calibre of the vein to be sclerosed. Then, using a screwing motion, we firmly block the tip of the syringe with a sterile hard plastic stopper usually used to seal perfusion tubes (fig. 1). The plunger of the syringe is

then pulled, creating a depression in it (fig. 2) causing, owing to the imperfect seal on glass syringes, aspiration and a very slight passage of air between the plunger skirt and the plunger itself which reaches the sclerosant solution "from behind" and immediately converting it into foam micro-bubbles (fig. 3), a mix of air and sclerosant. The traction must be firm and constant. If it is irregular, the micro-bubbles are of irregular calibre. The stronger the traction and therefore the faster the inrush of air, the larger the bubbles. Traction is gradually halted when the total volume of foam in the syringe reaches 3 cc (Fig. 4). The stopper is then removed and a 26 G 1/2 (0.45 x 12) or 30 G 1/2 (0.3 x 13) needle attached. Injection can begin. Very small volumes of foam (0.2-0.4 cc) are sufficient at each injection site.

Fig. 1 Hard plastic stopper

The average calibre of the micro-bubbles of foam is between 0.6 - 1.3 mm. The micro-foam is quite stable: Prepared at time H (calibre of bubbles: 1 mm), it can be modified at H + 1 hour (2 mm) or at H + 2 hours (2.8 mm).

It is easy to demonstrate an essential quality of the foam - its adhesiveness. When the syringe is full of foam, the stopper is removed from the tip and the syringe held vertically without a needle; the foam will not run out of the tip of the syringe unlike the solution. Similarly, whilst the level of bleeding when injecting varicose veins with solution is surprising, with the micro-foam this phenomenon is rare and, if it occurs, very much reduced. Moreover, in these cases, when the micro-foam injected into a varicose vein oozes out again, it displays the very fine calibre of the bubbles (< 1 mm). This strong adhesion by the micro-bubbles explains the enhanced efficacy of the foam in the treated varices at much lower concentrations and quantities.

RESULTS

From 6 November 1995 to 30 September 1998, we treated 10,263 patients (4 women to every 1 man) with an average age of 51 years (range: 8-93 years), i.e. around 70,000 injections (5-10 injections per session).

Sclerosis of reticular varices and varicose veins represents 80-85% of our phlebology work. The results with this type of pathology very soon confirmed to us what A. Monfreux had said: efficacy appeared entirely comparable to the solution with clear advantages and fewer disadvantages.

A/ Advantages

The benefits of foam sclerosis are many and are the main interest in it:

1) The injection (Fig. 5) is carried out using low or very low concentrations of sclerosant: 0.30-0.40% for reticular varices; 0.10-0.20% for varicose veins;

Fig. 2. Pulling the plunger, the tip obliterated by the stopper

Fig. 3. Micro-bubbles of foam

Fig. 4. Syringe filled with foam

2) The injection itself is very easy to carry out and requires no effort from the thumb maintaining pressure on the plunger;

3) There is triple monitoring of the injection:

- visually: the micro-bubbles compress the blood in the reticular varix or varicose vein which change colour or disappear;
- audibly: presence of a slight sputtering[1] sound during injection;
- by touch: if placed without any pressure along the course of the sclerosed vein, the finger can feel the passage of the micro-bubbles in the vessel.

  Once the needle is withdrawn, the level of bleeding (sometimes surprisingly prolific with the solution, especially with varicose veins) is slightly reduced or almost absent with the foam (Fig. 6);

4) The total quantity of sclerosant injected is less and offset by a substantially increased period of contact with the endothelium. The risks of inflammatory reaction, thrombosis at the injection site or pigmentation are thereby very much reduced;

5) In the event of extravascular injection, an instant, immediately visible "ballooning" occurs, immediately halting the injection. The quantity of sclerosant product issuing from the vessel is therefore substantially reduced and the local reaction less intense due to a weak concentration. Thrombectomies have become very rare;

6) The cost of sclerosis is substantially cut since the volume of sclerosant used is minimal.

Fig. 5. Injecting foam into a reticular varix

Fig 6. Injecting foam into a varicose vein

B/ Disadvantages

The disadvantages of using foam are minimal:

1) Only what are known as "tensio-active" sclerosants can produce foam: polidocanol and Thrombovar®. Iodine and Sclérémo® cannot be used;

2) It remains difficult to produce the foam using plastic syringes because there is no gap allowing air to pass between the plunger skirt and the plunger itself. Using glass syringes is currently recommended. Some people may worry about this practice and possible risks of contamination. Remember that it is imperative to wash syringes thoroughly after use, soak them in a disinfectant detergent such as Ampholysine® for 15 minutes, rinse them in clean water and leave them to dry. They must then be sterilised by passing through a partly loaded Poupinel with a thermal plate at 180° for one hour (but air is not a good heat vector) or, better still as it is more reliable, by a 1 1/4 hour cycle in an autoclave (with steam exposure plate at 138° for 10 minutes). It must be remembered that bacteria and the HIV virus are highly susceptible to heat. On the other hand, hepatitis viruses, especially hepatitis B, are more resistant, hence the importance of thorough sterilisation.

3) The tip of the syringe must be thoroughly obliterated so that "vacuum" in the body of the syringe is effective. After various trials, we selected a stopper model well adapted to this application, initially intended for sealing perfusion tubes, stable on the workbench, impervious and cheap. If elementary aseptic precautions are observed, a single stopper can be used for half a day in each treatment room.

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[1] Translator's note: being unsure what sound the injection makes, this may not be the correct word.

4) The preparation time for the micro-foam remains the most noticeable disadvantage to angiologists - around a minute for 3 cc. In fact, you need to be patient and exert constant traction on the plunger of the syringe over that time so as to obtain micro-bubbles of uniform calibre;

5) To restrict accidents, preferably no more than 3 cc of foam in total should be injected per session. If the situation demands it (arch, aversion by the patient, etc), 5 cc (i.e. two syringes) may be injected slowly followed by resting for 3-5 minutes in a semi-reclining position on the examining table.

COMPLICATIONS

The complications that marked the use of foam in our experiment are of various types:

- sight problems: 9 patients (of all ages) displayed sight problems almost immediately: 8 "impressions of spots before the eyes" lasting several minutes (with 2.5 cc and 5 cc); blindness in one eye lasting almost two hours (following injection of just 3 cc of foam) that was distressing to the female patient (aged 36 years) - and her therapist, especially as it occurred in the early days of our practice (early 1996);
- vomiting: 1 woman aged 49 years during the half hour after injection (4 cc);
- migraines: 7 female patients, generally young, not always with a known history of migraines;
- inflammations requiring a thrombectomy (fig. 7): common at the start of our experiment with the foam, especially if the injected dose exceeded 0.5 cc per site. Improved mastery of the technique soon made them very rare (one or two thrombectomies a week) and less severe, allowing them to be removed just with a needle (26 G);
- reduced, less intense pigmentation due to low concentration of sclerosing agent (fig. 8)
- "bad taste" sensation in the mouth: this unpleasant sensation is rare with polidocanol and exceptional if the latter is injected in the form of foam (2 cases in our practice);
- post-sclerosis ulceration, occurred in a female patient aged 52 years, 4 children, presenting with chronic evolutionary polyarthritis since April 1984 treated with corticosteroids, regularly monitored for sclerotherapy of the thighs and calves since 1985 (short bilateral crural stripping in 1984). Much improved, she complained of unsightly sclerosis of telangiectases on the internal surface of the right ankle where the skin was particularly thin without any sub-cutaneous cushion (post-cortisonal atrophy). Despite our reservations, we allowed ourselves to be persuaded by her arguments and her aesthetic demands and we completed one session (April 1996) with injections into the telangiectases in this ankle. There was no pain and no apparent incident. 42 days later, when attending a further session, the patient displayed 2 small necroses at the injection sites from the previous session. One developed scar tissue within 6 months and the other within 10 months leaving a slight depression in the skin at each point. This incident was the result of sclerotherapy being contraindicated. It shows that you have to be able to refuse the patient's demands when the local or general circumstances require it.

Fig. 7. Micro-thrombosis requiring a needle thrombectomy

Fig. 8. Slight pigmentation following foam sclerosis

A) Accident

Our only "accident" occurred with a woman aged 59 years, 3 children, teacher, benefited from previously sclerosis in 1983 (3 sessions), 1984 (3 sessions) and 1992 (1 session) for telangiectases (salicylate and sodium), without any significant reaction. On 25 August 1998, mid-morning, this patient consulted with a slight unilateral oedema of the left foot without any apparent aetiology; also pointing out the presence of several varicose veins on the right thigh, 8 injections of 0.30% foam (total 3 cc) were administered. In the minute following, the patient gave a vague impression of "malaise" which appeared to lessen. However, when she got down from the table 3 minutes later, she fell without losing consciousness. She then noted "pins and needles" in her left arm and hand lasting 5 minutes (without motor deficit) and then in the right at the same points. Despite "a difficulty in expressing herself", she remained perfectly intelligible. After lying down in the surgery for an hour and a half before all symptoms disappeared, she returned home "feeling fine". In the afternoon, headaches occurred accompanied by two brief episodes of vomiting which occurred again the next day. The multiple tests carried out at the time, especially in the neurological area, did not show any abnormality. We learnt little here but faced with the appearance of new symptoms (drunken gait, vertigo, etc) and recent MRI anomalies, the diagnosis of early plaque sclerosis was considered. Despite very low doses and concentrations can this "accident" on 25 August 1998 be attributed to the foam?

DISCUSSION

Polidocanol foam sclerotherapy carried out extemporaneously using air had not been the subject of other publications in December 1996.

By contrast, Juan R. Cabrera Garrido et al had reported (6) in May 1996 on their experiment with a micro-foam produced using polidocanol and CO_2 and injecting it via an intrasaphenous catheter with promising results in sclerosis of saphenous trunks and in certain vascular deformities (haemangiomae). However, the procedure for obtaining the foam is not described and appears to require prior recourse to a pharmacist, excluding extemporaneous preparation at the surgery.

At the World Congress of Phlebology in Sydney in September 1998, J.P. Benigni et al (7) reported on a comparative, prospective, randomised, open pilot study demonstrating optimum efficacy from Aetoxisclerol® foam compared to the solution but in a small group, and S. Sadoun (8) described a "small-scale" process allowing the foam to be produced using plastic syringes by creating strong traction on the syringe plunger and then releasing it suddenly and doing this several times in a row. Doubtless, in the near future there will be a more satisfactory system of producing the foam in plastic syringes.

We are well aware that our subjective, non-quantified experiment reported here is only of relative value but it will have had the merit of broadcasting among the medical profession a new sclerotherapy procedure and engaging protocols for prospective, randomised studies into scientifically indisputable results.

CONCLUSION

Between 6 November 1995 and 30 September 1998, we used only polidocanol foam for sclerosant injections into reticular veins and telangiectases. Results have appeared excellent with minimal, rare adverse effects if the concentrations and, especially, the injected volumes are reduced.

This effective method that is easy to carry out, straightforward and well tolerated represents a marked improvement in sclerotherapy techniques and deserves to be shared more widely among the angiology community.

Validating the results remains the outstanding goal over the next few years, even if this is difficult to achieve.

BIBLIOGRAPHY

1. One year of daily application of sclerotherapy (reticular veins and telangiectases) using polidocanol foam: feasibility, results, complications.

6. Pushing the boundaries of sclerotherapy: new sclerosing products.